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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/632,794	08/04/2003	Hui-Jen Tsai	8961-000004/US	5554
30596 7590 03/17/2008 HARNESS, DICKEY & PIERCE, P.L.C. P.O.BOX 8910 RESTON, VA 20195				
EXAMINER BERTOGLIO, VALARIE E				
ART UNIT		PAPER NUMBER		
1632				
MAIL DATE		DELIVERY MODE		
03/17/2008		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/632,794

Applicant(s)

TSAI, HUAJEN

Examiner

Valarie Bertoglio

Art Unit

1632

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 September 2007 and 08 November 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 3 and 7 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 3 and 7 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 04 August 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/24/2007 has been entered.

Specification

Applicant's amendment to the specification dated 09/24/2007 is noted. The objection to the amendment filed 01/06/2007 under 35 U.S.C. 132(a) because it introduces new matter into the disclosure is withdrawn.

Claim Objections

The previous objections to the claims are withdrawn in light of Applicant's amendments to the claims.

Double Patenting

The double patenting/duplicate claims warning is rendered moot as Applicant has cancelled the relevant claims.

Claim Rejections - 35 USC § 112-2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 1-5,7,8 and 10-12 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in light of Applicant's amendments to, or cancellation of, the claims.

Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "on skeletal muscle" is unclear as it is not known whether the claim is requiring deposition of the RFP on the muscle or just expression in the cells of the muscle. The claim is also unclear because it is drawn to a product according to the method of claim 3. It is unclear if the claim is referring to a product made by the method of claim 3 or a particular product used in the method of claim 3.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

1) Claims 3 and 7 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Hsiao et al. [2001] in view of Carvan et al [2000] and further in view of Finley et al, [Biotechniques, 31:66-72, July 2001]. The rejection is maintained for reasons of record set forth at pages 11-12 of the office action dated 03/03/2006 (note the rejection was applied to claims 3 and 7 at page 7 of the office action dated 03/23/2007).

The rejection of claims 4-12 is rendered moot by the cancellation of the claims.

Applicant's arguments have been fully considered and are not persuasive.

Applicant argues that Hsiao does not teach or suggest the use of a red fluorescent protein and that Carvan, while teaching red fluorescent protein, does not teach such in stable transgenics (page 7, paragraph 4-page 8, paragraph 2 of Applicant's Remarks).

In response, it is noted that Carvan taught use of golden zebrafish, not red fluorescence. Carvan taught the use of *golden* mutants to make transgenic zebrafish comprising transgenes encoding fluorescent products (page 141, paragraph 5), Carvan taught that golden mutants are preferred over other pigmentation mutants, such as *albino*, because *albino* mutants are poor breeders.

Applicant argues that Carvan taught that there are difficulties in sustaining transgene expression beyond the F2 generation in zebrafish (page 8, paragraph 2 of Applicant's Remarks).

In response, the phenomenon discussed by Carvan is relevant to use of non-fish promoters and constructs. On the contrary, much success has been found in germline transmission of active transgenes comprising native fish sequences in zebrafish through multiple generations. Carvan is relied upon for the suggestion of using golden zebrafish to better visualize fluorescence.

With respect to Applicant's arguments regarding the teaching of Opsahl (paragraph bridging pages 8-9 of Applicant's Remarks) that different strains of mice can express a transgene differently, there is no reason to believe the phenomenon observed in mice would hold true for fish (see page 12 of the final office action dated 03/23/2007). With respect to position effects (paragraph bridging pages 9-10), this phenomenon is readily dealt with through obtaining multiple transgenic lines with independent insertion events.

More specifically, Applicant argues that the Examiner has not provided evidence that the differences in expression of some transgenes between mouse strains would not occur in fish species. In

response, in turn, Applicant has provided no evidence that any significant difference of the claimed transgene would be expressed differently in different strains of fish. OPSahl taught that *some* transgenes in *some* strains of *mice* are expressed in a somewhat different patten. There is no evidence on the record that the specifically claimed α -actin promoter would not be expressed substantially in the same manner in the claimed *golden* backgroun as it is in the leopard genetic background taught by Hsiao. Thus, there would be no reason to not substitute the *golden* strain of Carvan for the *leopard* strain of Hsiao as asserted by Applicant.

As for substitution of DsRed for EGFP (pages 1011 of Applicant's Remarks), it was standard, well-known, and well-accepted in the art at the time of filing to interchange any gene encoding a fluorescent protein (GFP, RFP, CFP, BFP, etc) both in vitro and in vivo and such a specific teaching is not necessary to render obvious the combination of in vivo fluorecence taught by Hsiao et al with the fluorescent gene product encoded by DsRed2 taught by Living Colors. In light of the common, routine and accepted state of the art at the time of filing, there is no evidence suggesting replacing EGFP of Chou et al with DsRed2 of Living Colors would be anything other than routine. It is also noted that the ornamental value of the fish is of no relevance to the instant claims.

2) Claim 1 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Hsiao et al. [2001] in view of Finley et al, [Biotechniques, 31:66-72, July 2001]. The rejection is maintained for reasons of record set forth at pages 14-16 of the office action dated 03/23/2007 and reiterated below.

The rejection of claim 2 is rendered moot by the cancellation of the claim.

Hsiao taught a method of making a transgenic zebrafish with systemic fluorescence of the skeletal musculature by injecting a linearized plasmid including flanking ITRs, an α -actin promoter that replaced a CMV promoter, a fluorescent EGFP gene and an SV40 polyA, into fertilized zebrafish embryos (Figure 1, second construct; page 325, col. 2, paragraph 2; page 333, col. 2, paragraphs 1 and 3).

Hsiao *et al.* did not teach use of a gene encoding a red fluorescent protein.

However, Finley *et al.* taught the use of several different fluorescent reporters in zebrafish, including DsRed. Finley also taught properties unique to DsRed such as low turnover and a unique emission spectra. Furthermore, Finley *et al.* taught that DsRed has a high signal to noise ratio, optimizing it as a reporter gene.

It would have been obvious to one of ordinary skill in the art at the time of filing to combine the technology taught by Hsiao of using ITR elements to enhance fluorescent reporter gene expression in transgenic zebrafish with the teachings of Finley regarding use of DsRed as a fluorescent reporter. One of skill in the art would have been motivated to combine these teachings of Hsiao *et al.* with those of Finley *et al.* because Finley *et al.* taught advantages of DsRed over GFP as well as uses for multiple fluorescent reporter genes in the same fish.

Applicant's arguments to the preceding rejection of claims 3 and 7 under 35 USC 103(a) are relevant to the instant rejection. These arguments are addressed above and applicable to the instant rejection.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Valarie Bertoglio, Ph.D./
Primary Examiner
Art Unit 1632

